REMARKS/ARGUMENTS

By the present amendment, claim 1 has been amended to incorporate the subject matter of previous claims 3, 5-7 and 9 which have been canceled. Claims 12 and 22 have been amended to specify that the starting cells are stem cells or progenitor cells. A new claim 29 has been added which incorporates the subject matter of previous claims 3 and 5-7 and further specifies that the stromal cells are murine and that the system induces murine T lymphopoiesis. Support for this amendment can be found on page 16, line 18 as well as in the examples. New claims 30-43 find support in original claims 2, 4, 8-17, 22 and 24. The amendments to the claims have been made without prejudice and without acquiescing to any of the Examiners objections. Applicant reserves the right to pursue any of the deleted subject matter in a further divisional, continuation or continuation-in-part application. The amendment does not contain new matter and its entry is respectfully requested.

The Official Action dated January 25, 2005 has been carefully considered. It is believed that the amended specification and claims and the following comments represent a complete response to the Examiner's rejections and place the present application in condition for allowance. Reconsideration is respectfully requested.

I. 35 USC §112, First Paragraph

The Examiner has objected to claims 1-17, 22 and 24 under 35 USC §112, first paragraph as lacking enablement for an *in vitro* system comprising any stromal cells expressing any Notch ligand that supports any and all T cell lymphopoiesis from any cell but does not support B cell lymphopoiesis. The Examiner raises several distinct objections and we will discuss each in turn below.

a) Stromal Cells

The Examiner alleges that the specification only provides guidance on the use of OP9 stromal cells. Currently, amended claims 1, 2, 4, 8, 10-17, 22 and 24 specify

that the stromal cells are OP9 stromal cells. Consequently, the objection to these claims is overcome.

Newly submitted clams 29-43 specify that both the stromal cells and the starting cells that undergo T cell lymphopoiesis are of murine origin. The Examiner states that Delta-like-1 expressing S-17 stromal cells are unable to produce mature differentiated T cell lineages. The results in Example 9 demonstrate that S-17 cells can promote T cell lymphopoiesis when used on murine cells.

In view of the foregoing, we respectfully submit that the application enables the use of OP9 stromal cells to produce any type of T cell as well as the use of murine stromal cells to produce murine T cells.

b) Notch Ligands

The Examiner is of the opinion that the specification only enables the use of Delta-like-1 ligands. The claims, as amended herewith, specify stromal cells expressing DL-1 or DL-4 Notch ligands. The Examiner has confirmed the enablement for DL-1 ligands. With respect to DL-4 ligands, there is support in Examples 1 and 3 that DL-4 can induce T cell differentiation.

In view of the foregoing, we respectfully submit that the application enables the use of DL-1 and DL-4 ligands.

c) T Cell Lineages

The Examiner is of the opinion that the specification does not enable the development of all T cell lineages. Specifically, the Examiner states that the Examples do not demonstrate that αβ CD4+CD8- T cells can be developed using the *in vitro* system. We respectfully disagree as one of skill in the art could readily determine how to modify the system in order to produce the αβ CD4+CD8- T cells. As noted by Rothenberg, which was cited by the Examiner in the office

action, this subset of T cells is likely not produced because the system does not include an MHC class II molecule. This is also noted in the Lehar review also cited by the Examiner. Therefore, one of skill in the art would readily know to include MHC class II molecules if they wanted to produce αβ CD4+CD8- T cells. This would not require undue experimentation. The Courts have held that some experimentation is permissible to "adapt the invention to particular settings" (See Fields v. Conover, 1971 CCPA). In the present case, providing MHC class II molecules is merely adapting the invention to a specific situation when αβ CD4+CD8- T cells are desired.

In view of the foregoing, we respectfully submit that the application enables the preparation of all T cells.

d) Starting Cells

The Examiner is of the opinion that the specification does not enable the preparation of T cells from any and all cells. The Examiner specifically states that the working examples do not describe that terminally differentiated cells such as fibroblasts, melanocytes or epithelial cells can be induced to form T cells, at any stage. We respectfully submit that one of skill in the art would not use fully differentiated cells to form T cells. Further, for greater clarity, claims 12 and 22 have been amended to specify that the cells that are cultured are stem cells or progenitor cells, both of which have the capability to form mature T cells in the system of the present invention.

The Examiner also states that the specification does not teach that any species of embryonic stem cells can be used in the *in vitro* system to form T cells. Applicants are not claiming novel embryonic stem cells but rather a novel assay that allows the development of T cells. One of skill in the art can readily determine which starting cells can be used in the system. We do not dispute that isolating or identifying stem cells from all mammals is still an area of active research.

Nevertheless, one of skill in the art would use stem cells that are readily available at the time they wish to conduct the method of the invention.

In view of the foregoing, we respectfully submit that the application enables the preparation of T cells from all progenitor or stem cell types.

In view of the foregoing, we respectfully request that all of the objections to the claims under 35 USC §112, first paragraph, be withdrawn.

II. Double Patenting

The Examiner has objected to claims 1-17, 22 and 24 under 35 USC §101 as claiming the same invention as copending No. US 10/731,741. We do not understand this objection as US 10/731,741 is the present application.

In view of the foregoing, we respectfully request that the objections to the claims under 35 USC §101 be withdrawn.

III. 35 USC §102

The Examiner has objected to claims 1-7, 12-15, 17 and 22 under 35 USC §102(b) as being anticipated by Jaleco et. al. (Journal of Experimental Medicine, 2001).

Jaleco et al. describes using S17 stromal cells that express Delta-1 to induce T cell lymphopoiesis of human stem cells. As mentioned previously, independent claim 1 has been amended to specify OP9 cells expressing a Delta-like-1 or Delta-like-4 ligand. New claim 29 specifies the use of murine stromal cells to support murine T cell lymphopoiesis. The remaining claims depend either directly or indirectly from claim 1 or 29. As a result, all of the amended claims are novel over Jaleco et. al.

In view of the foregoing, we respectfully request that the objections to the claims under 35 USC §102(b) be withdrawn.

The Commissioner is hereby authorized to charge any fee (including any claim fee) which may be required to our Deposit Account No. 02-2095.

In view of the foregoing comments and amendments, we respectfully submit that the application is in order for allowance and early indication of that effect is respectfully requested. Should the Examiner deem it beneficial to discuss the application in greater detail, he is kindly requested to contact the undersigned by telephone at (416) 957-1682 at his convenience.

Respectfully submitted,

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